

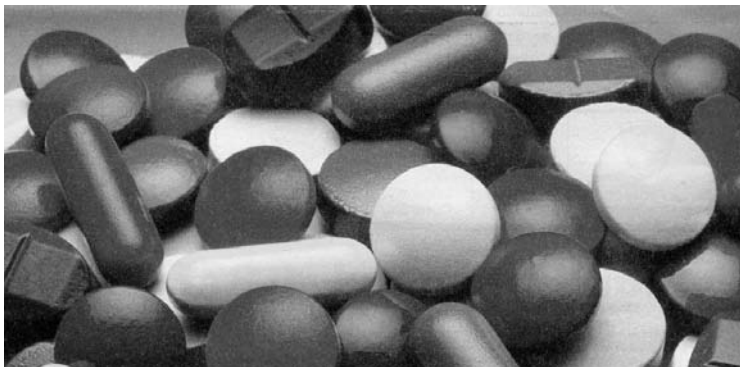
CMC Certification Review



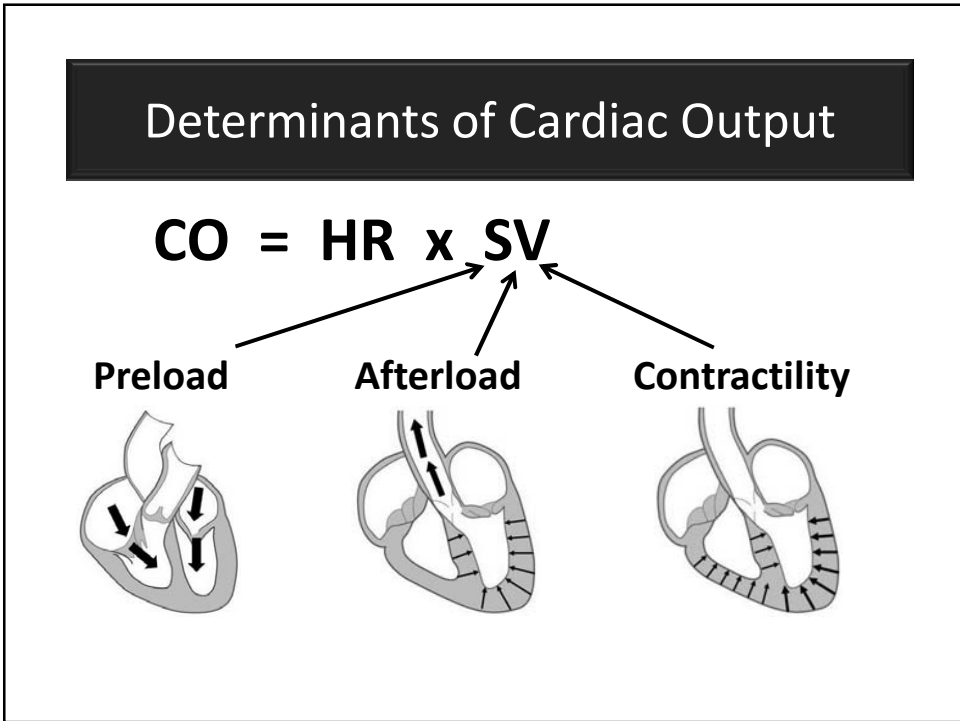
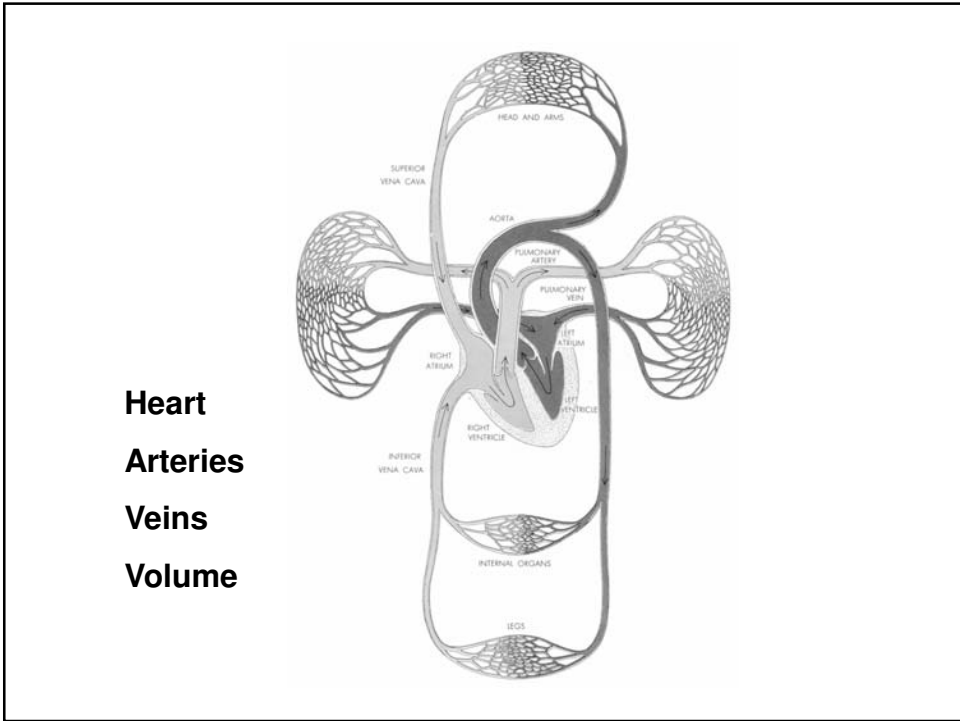
Cardiovascular Nursing Education Associates

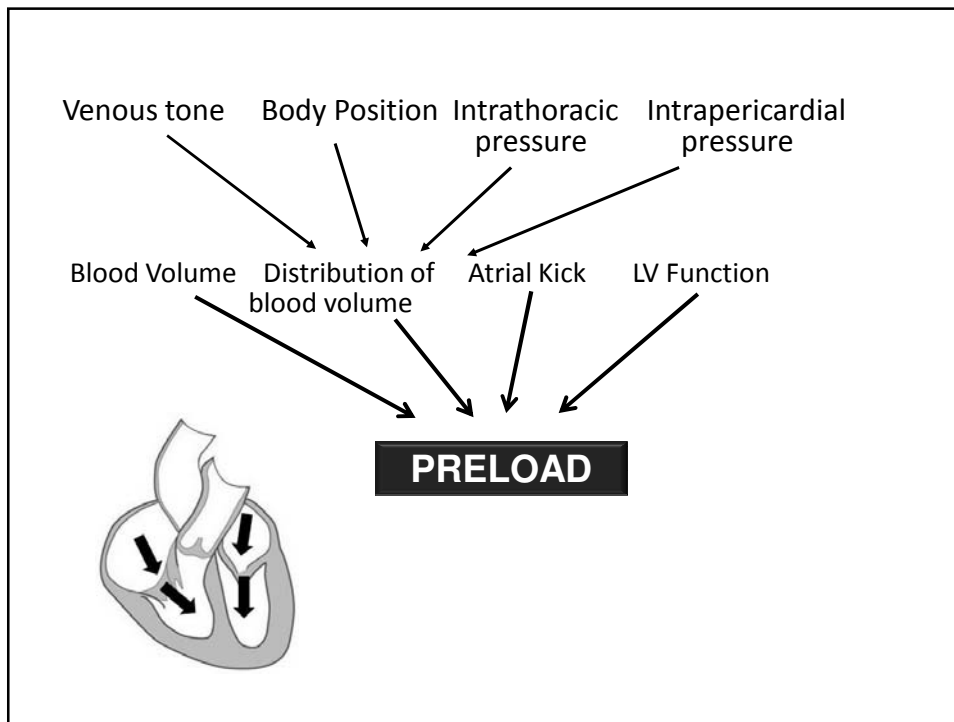
Carol Jacobson RN, MN
Karen Marzlin RN, CCRN, CMC
Cindy Webner RN, CCRN, CMC

Cardiovascular Drugs: Why We Use What We Use



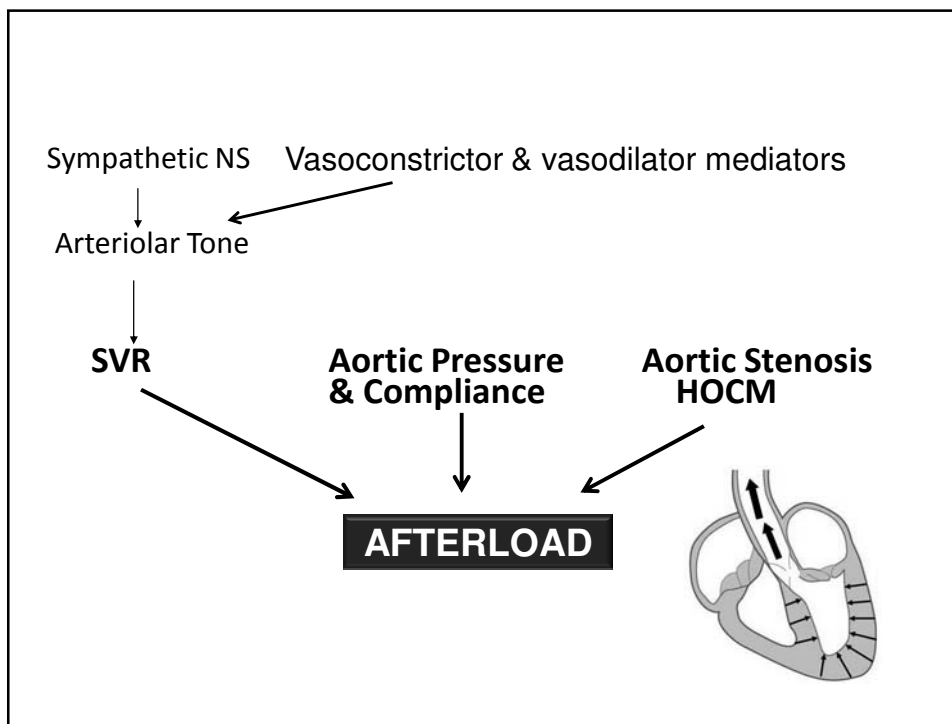
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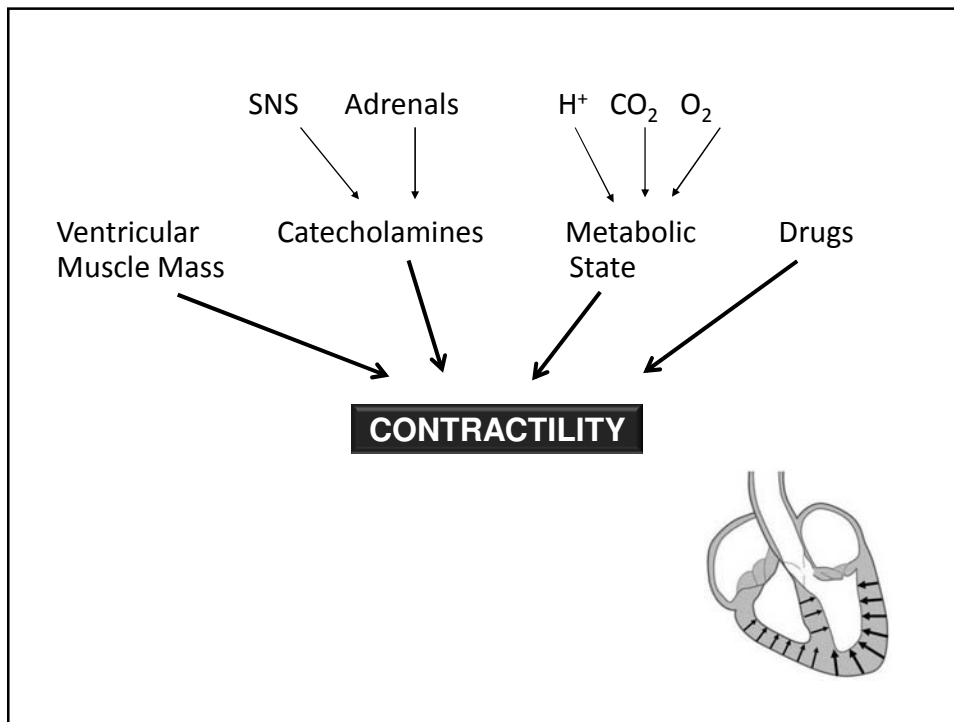
Conditions That Alter Preload

- Hypovolemia
 - Hemorrhage
 - Dehydration
 - Burns
 - Overdiuresis
 - Third Spacing
- Hypervolemia
 - Overhydration
 - CHF
 - Renal disease
- Altered Size of Vascular Space
 - Sepsis
 - Spinal or epidural anesthesia
 - Anaphylaxis
 - Venous dilating drugs
 - NTG
 - ACEI, ARBs
 - Nesiritide



Conditions That Alter Afterload

- **Vasodilation**
 - Sepsis
 - Spinal or epidural anesthesia
 - Anaphylaxis
 - Arterial dilating drugs
 - Nipride
 - ACEI, ARBs
 - Nesiritide
 - Milrinone
 - Ca⁺⁺ channel blockers
 - Antihypertensives
- **Vasoconstriction**
 - Hypertension
 - Compensatory vasoconstriction
 - Drugs
 - Neosynephrine
 - Levophed
 - High-dose dopamine
 - Epinephrine
 - Vasopressin

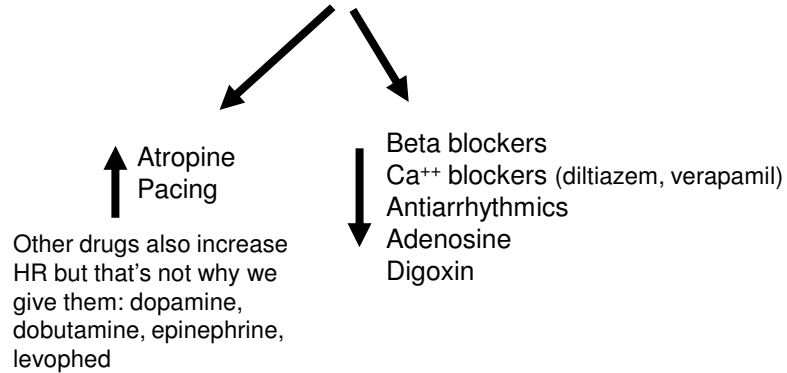


Conditions That Alter Contractility

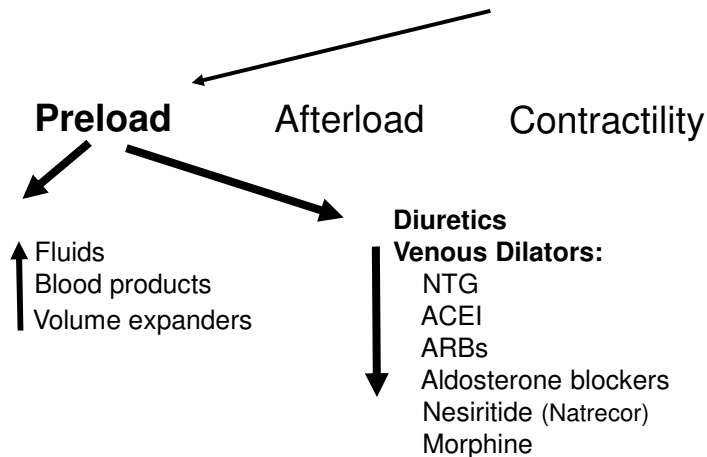
- Increase
 - Pheochromocytoma
 - Hyperthyroidism
 - Positive inotropic drugs
 - Dobutamine
 - Dopamine
 - Levophed
 - Milrinone
 - Digoxin
- Decrease
 - Myocardial infarction
 - Cardiomyopathy
 - Ischemia
 - Hypoxia
 - Acidosis
 - Negative inotropic drugs
 - Beta blockers
 - Ca⁺⁺ blockers
 - Antiarrhythmics
 - Some chemo agents
 - Some anesthetics, sedatives

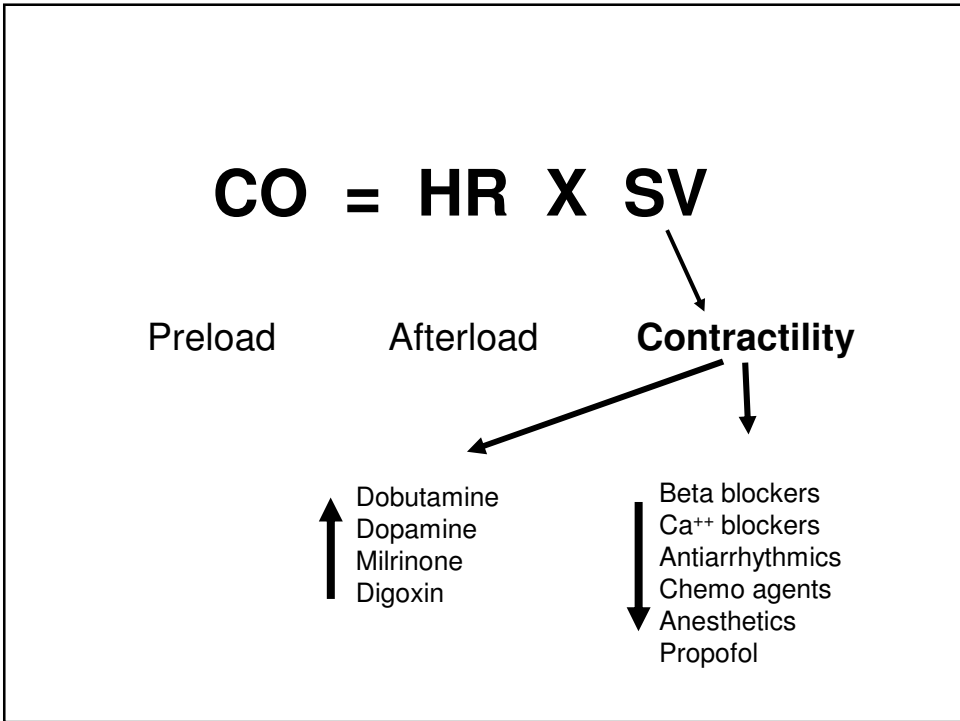
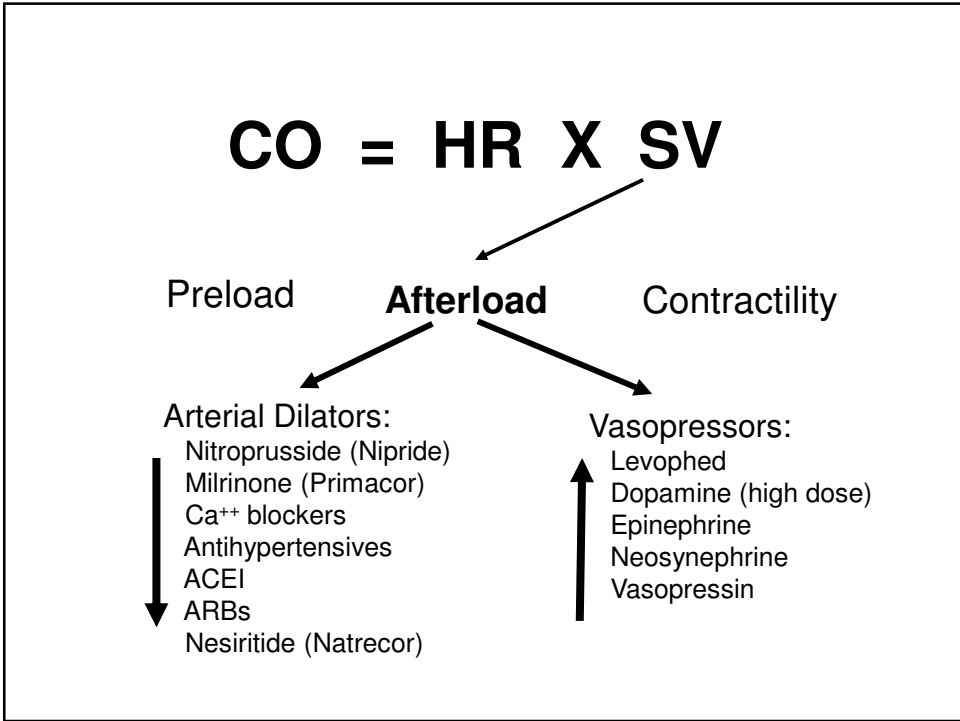
Therapy to Alter CO

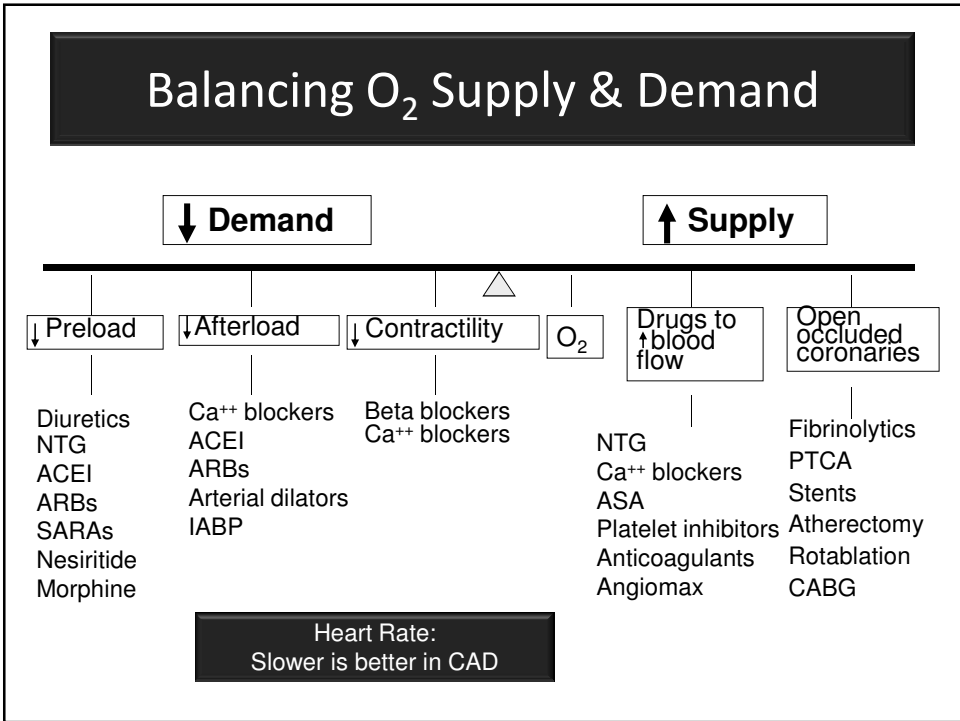
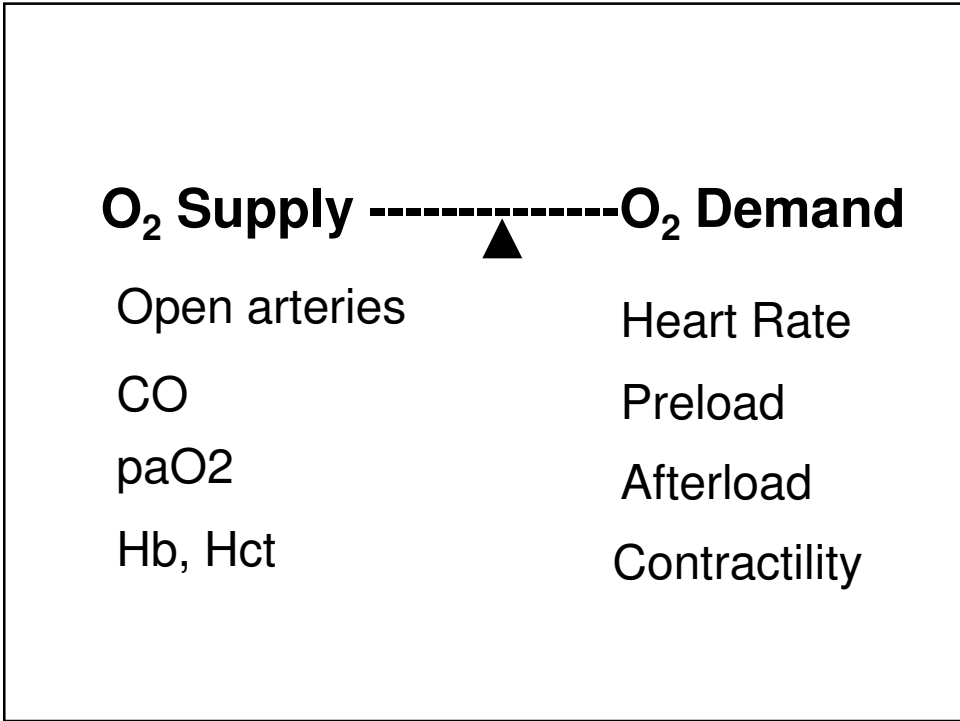
$$\text{CO} = \text{HR} \times \text{SV}$$



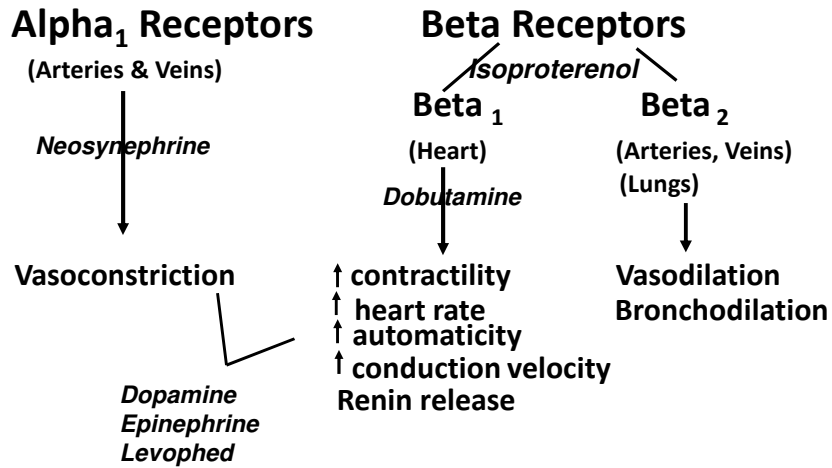
$$\text{CO} = \text{HR} \times \text{SV}$$



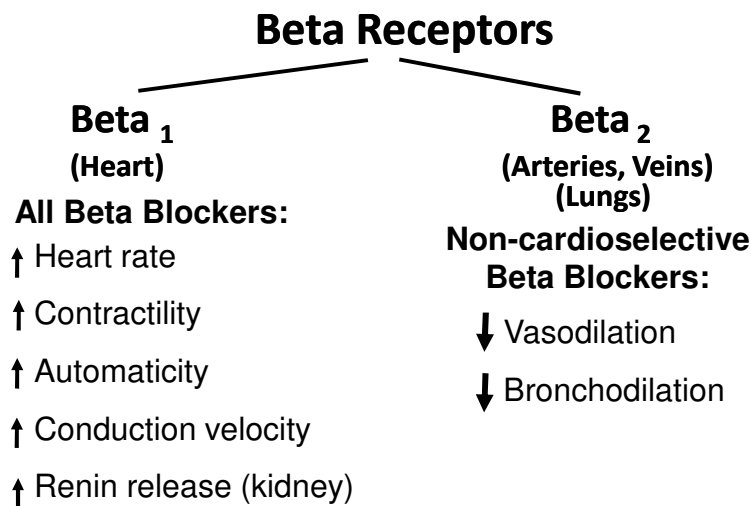




Sympathetic Nervous System & Sympathomimetic Drugs



Effects of Beta Blockers



Clinical Use of Beta Blockers

Use	Mechanism of Action
Hypertension	↓ heart rate = ↓ CO = ↓ BP ↓ contractility = ↓ CO = ↓ BP BP = CO x SVR ↓ renin release in kidney = ↓ angiotensin II formation
Classic Angina	↓ O ₂ demand by ↓ HR, ↓ contractility, ↓ BP ↑ O ₂ supply by ↓ HR which ↑ diastolic filling and coronary perfusion time
Acute MI MI Follow-up	↓ automaticity in ventricle so ↓ risk of VF early in MI Preserves ischemic myocardium by ↓ O ₂ demands
Arrhythmias	↓ automaticity so ↓ VT, VF ↓ AV conduction to slow ventricular rate in A Fib or flutter, may terminate PSVT
Hypertrophic Cardiomyopathy	↓ contractility so reduces outflow tract obstruction ↓ HR allows longer diastolic filling time, more blood in ventricle decreases outflow tract obstruction
Migraines	Inhibits β mediated vasodilation in cerebral vessels

Side Effects of Beta Blockers

- **Cardiac**
 - Bradycardia, AV block
 - Heart failure
 - Hypotension
- **Pulmonary**
 - Bronchoconstriction
 - Pulmonary edema
- **Peripheral Vascular**
 - Vasoconstriction
- **Metabolic**
 - Mask signs of hypoglycemia
 - Augment hypoglycemic actions of insulin
 - Increase serum triglycerides
- **Other**
 - Fatigue, sleep disturbances
 - Depression
 - Sexual dysfunction
 - Weight gain

Beta Blockers

- **Nonselective: Block both Beta₁ & Beta₂**

Propranolol (Inderol)	Nadolol (Corgard)
Timolol (Blocadren)	Sotalol (Sotacor)
Penbutolol (Levatol)	Oxprenolol (Trasicor)

- **Cardioselective: Block Beta₁**

Acebutolol (Sectral)	Atenolol (Tenormin)
Metoprolol (Lopressor)	Esmolol (Brevebloc)
Bisoprolol (Zebeta)	Nebivolol (Bystolic)

- **Combined Alpha & Beta Blocking:**

Labetalol (Trandate, Normodyne)
Carvedilol (Coreg)

Effects of Ca⁺⁺ on Heart & Blood Vessels

- Depolarization of SA node and AV node cells (“slow current” calcium dependent cells)
- Facilitates contraction of heart and smooth muscle layer of blood vessels
 - Facilitates actin-myosin interaction in muscle)



Effects of Ca⁺⁺ Channel Blockers

- **Heart:**
 - ↓ **heart rate** (except Nifedipine-like agents)
 - ↓ **AV conduction velocity**
 - ↓ **contractility**
- **Blood Vessels:**
 - Coronary vasodilation** (prevent vasospasm)
 - Peripheral vasodilation** (afterload reduction)

Side Effects of Ca⁺⁺ Channel Blockers

- Bradycardia (verapamil, diltiazem)
- AV Block (verapamil, diltiazem)
- Hypotension (especially nifedipine)
- Heart Failure (especially Verapamil)
- Flushing, headaches
- Peripheral edema
- Constipation (especially verapamil)

Clinical Uses of Ca⁺⁺ Channel Blockers

Use	Mechanism of Action
Angina: Coronary Spasm Classic Angina	Prevents vasoconstriction by decreasing amount of Ca ⁺⁺ available for contraction. Coronary vasodilation increases collateral blood flow. ↓MVO ₂ by ↓HR, ↓contractility, ↓afterload
Hypertension	↓CO by ↓contractility, ↓SVR by vasodilation BP = CO x SVR
Arrhythmias: SVT	Slows AV conduction so ↓ventricular response to atrial fib & flutter. Can terminate AV nodal active arrhythmias.
Hypertrophic Cardiomyopathy	↓contractility lessens outflow tract obstruction. ↓HR allows longer diastolic filling time, more blood in ventricle keeps outflow tract open

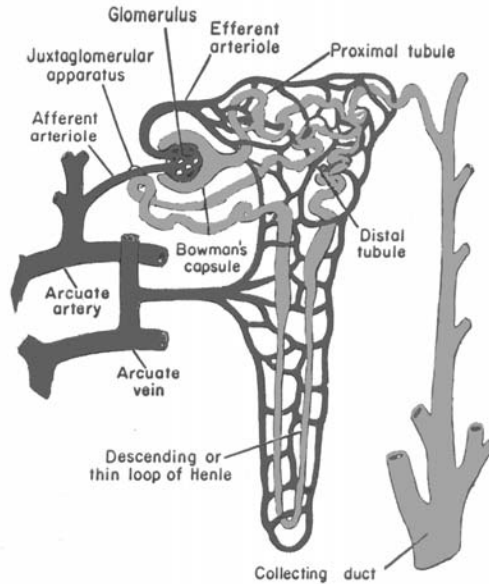
Ca⁺⁺ Channel Blockers

- **Heart Rate Lowering:**
 - Verapamil (Calan) – most depression of contractility
 - Diltiazem (Cardizem)

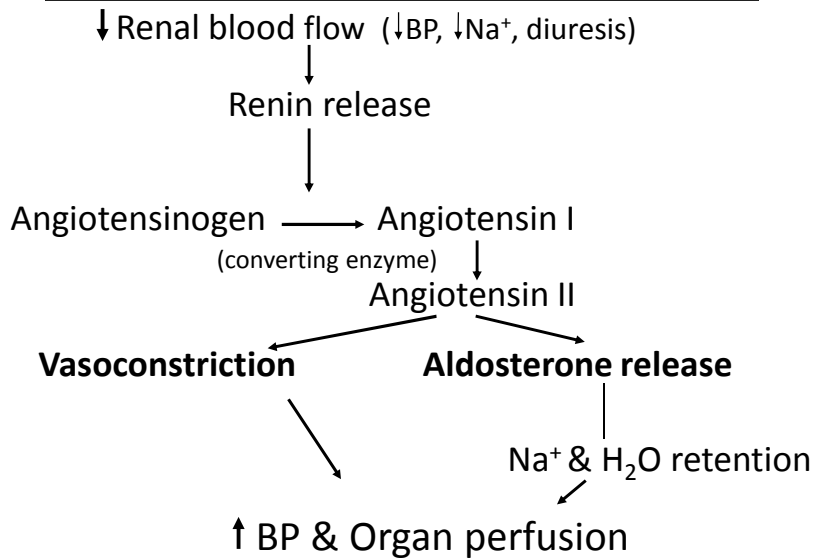
- **Dihydropyridines** (potent vasodilators, little or no depression of contractility)
 - Nifedipine (Procardia, Adalat) – short acting, comes in sustained release form for longer action
 - Felodipine (Plendil)
 - Isradipine (DynaCirc)
 - Nisoldipine (Sular)
 - Amlodipine (Norvasc) – long acting, no cardiac depression, safest one in HF

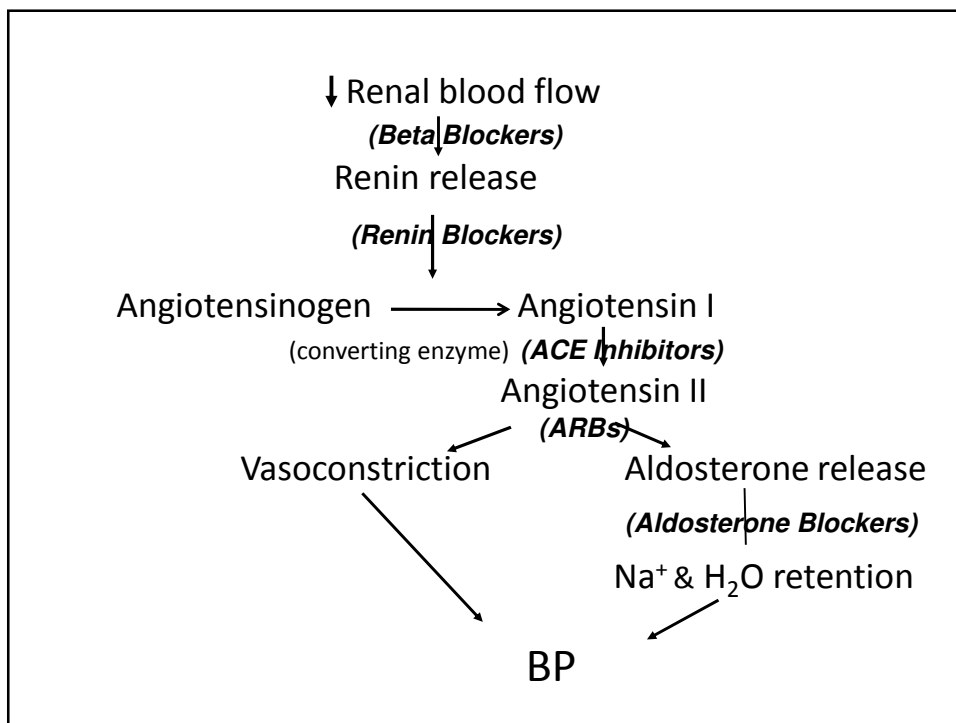
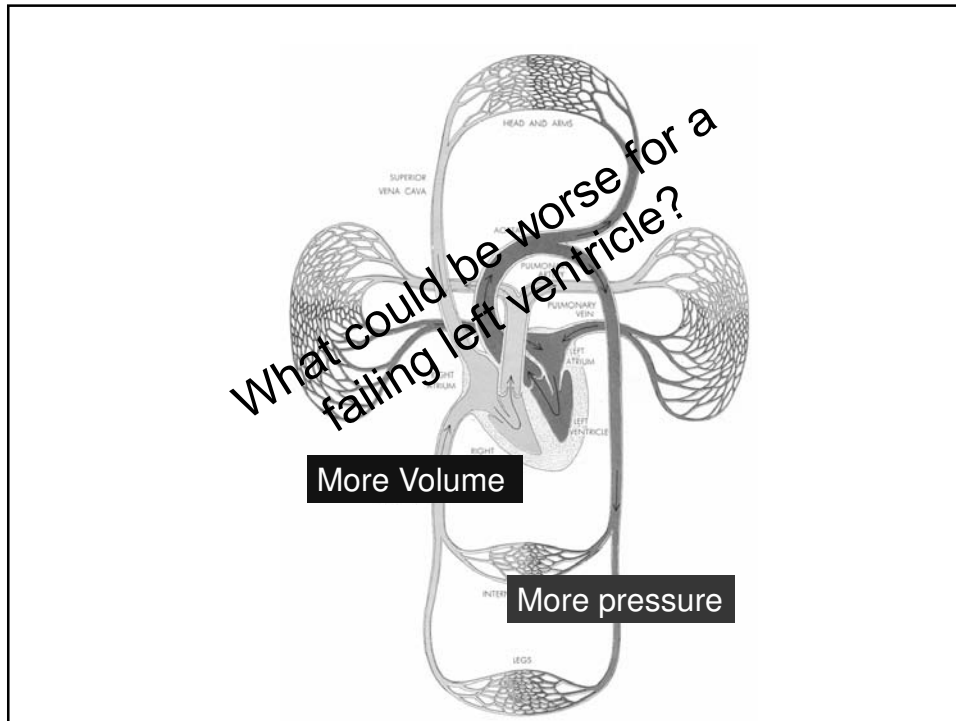
Longer acting, little cardiac depression

Role of Kidney in HF

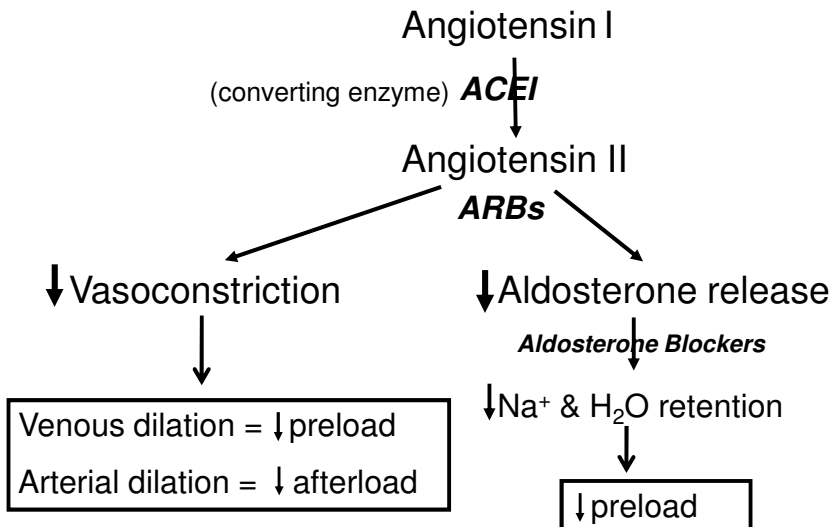


Renin-Angiotensin System





Hemodynamic Effects



BP = CO x SVR

- BP value does not tell you WHY the BP is low
 - Must evaluate determinants of BP and treat the cause
- Low BP could be due to:
 - Low CO
 - HR too slow or too fast
 - Preload too low or too high
 - Contractility low
 - Low SVR
 - Vasodilation due to sepsis, drugs, anaphylaxis

Drug Therapy to Decrease BP

$$\downarrow \text{BP} = \downarrow \text{CO} \times \downarrow \text{SVR}$$

Drugs to \downarrow CO

- Diuretics
- Beta Blockers (“olols”)
- Calcium Channel Blockers

Drugs to \downarrow SVR

- Peripheral Alpha Blockers (prazosin, terazosin, regitine etc)
- Direct Arterial Dilators (hydralazine, minoxidil)
- ACEI (“prils”), ARBs (“sartans”)
- PDE inhibitors (milrinone)
- Calcium Channel Blockers (“pines”: amlodipine, felodipine, etc)
- \uparrow nitric oxide in vascular tissue (nitroprusside, nitrates)
- Centrally Acting Agents (clonidine, guanabenz, guanfacine)

Drug Therapy to Increase BP

$$\uparrow \text{BP} = \uparrow \text{CO} \times \uparrow \text{SVR}$$

Drugs to \uparrow CO

- Volume
- Inotropes
 - Dobutamine
 - Dopamine
 - Milrinone

Drugs to \uparrow SVR

- Vasopressors
 - Levophed
 - Neosynephrine
 - Vasopressin
 - Epinephrine
 - Dopamine

Drug Therapy for Hypertension

- Thiazide diuretics (chlorthalidone, HCTZ)
- ACE Inhibitors / ARBs
- Calcium blockers
- Beta blockers

The amount of blood pressure reduction is the major determinant of reduction in cardiovascular risk, not the choice of antihypertensive drug.

Diuretics

Thiazides

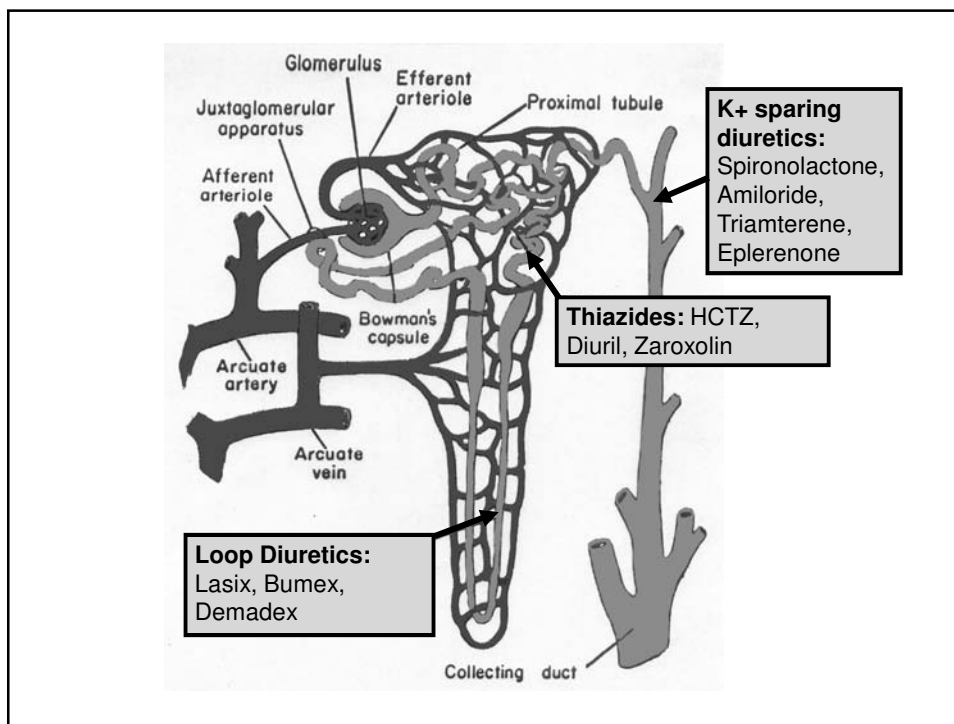
- Chlorothiazide (Diuril)
- Chlorthalidone (Hygroton)
- Hydrochlorothiazide (HydroDiuril)
- Polythiazide (Renese)
- Indapamide (Lozol)
- Metolazone (Zaroxolyn)

Loops

- Bumetanide (Bumex)
- Furosemide (Lasix)
- Torsemide (Demadex)

K⁺ Sparing

- Amiloride (Midamor)
- Triamterene (Dyrenium)
- Spironolactone (Aldactone)
- Eplerenone (Inspra)



Thiazides

- Most common first-line therapy for HTN (especially in elderly and African Americans)
- Inhibit Na⁺ reabsorption in distal tubule
- Less potent than loops
- Longer duration of action than loops (6-12 hours), diuresis occurs in 1-2 hours
- Ineffective in presence of renal failure
- "Low ceiling" = maximal response reached at relatively low doses
- May take several weeks to become effective

Loops

- Agents of choice in HF and acute pulmonary edema
- Cause excretion of Na⁺ in ascending limb of loop of Henle
- Effective even in presence of renal failure
- Rapid onset of IV form (10-20 minutes)
- "High ceiling" – increasing response with increasing dose
- Potent diuretic activity (relatively greater urine volume and less loss of Na⁺ than thiazides)
- Need to be taken twice a day in HTN due to short half life

Side Effects of Diuretics

Thiazides

- Hypokalemia
 - May contribute to ventricular arrhythmias
- Hypomagnesemia
- Hyperglycemia (insulin resistance)
- Increased uric acid levels (gout)
- Increased cholesterol and triglyceride levels
- Impotence
- Hypotension
- Lethargy
- Nausea, dizziness, headache

Loops

- Hypokalemia, hypocalcemia, hypomagnesemia
- Hyperglycemia
- Increased cholesterol and triglyceride levels
- Increased uric acid levels (gout)
- Alkalosis
- Deafness (high doses)
- Skin reactions (photosensitivity, rashes)

K+ Sparing

- Hyperkalemia
- Hyponatremia
- Gynecomastia
- Sexual dysfunction
- Menstrual problems
- Headache
- Fatigue
- Dizziness

Inotropes

- Dobutamine
- Milrinone [Primacor]
- Dopamine
- Epinephrine
- Norepinephrine [Levophed]
- Digoxin

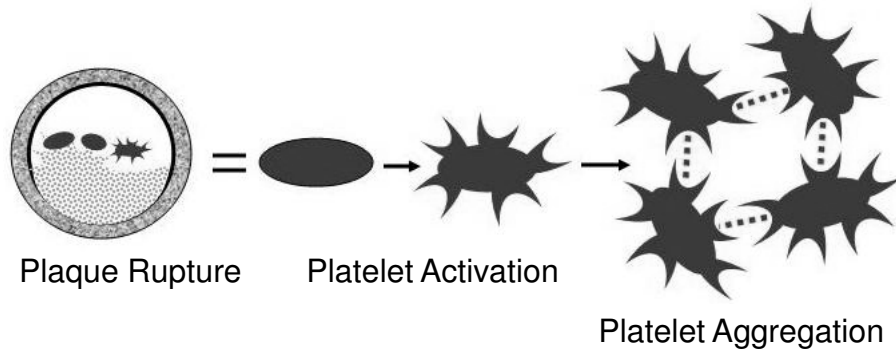
Vasodilators

- Nitroprusside [Nipride] (arterial, venous)
- Nitroglycerin (mostly venous)
- Ca⁺⁺ blockers ["pines"]
- Milrinone [Primacor]
- ACE Inhibitors ["prils"]
- ARBs ["sartans"]
- Hydralazine [Apresoline]

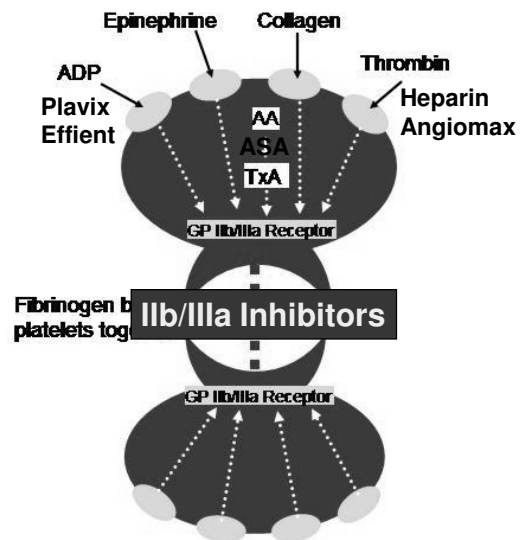
Vasopressors

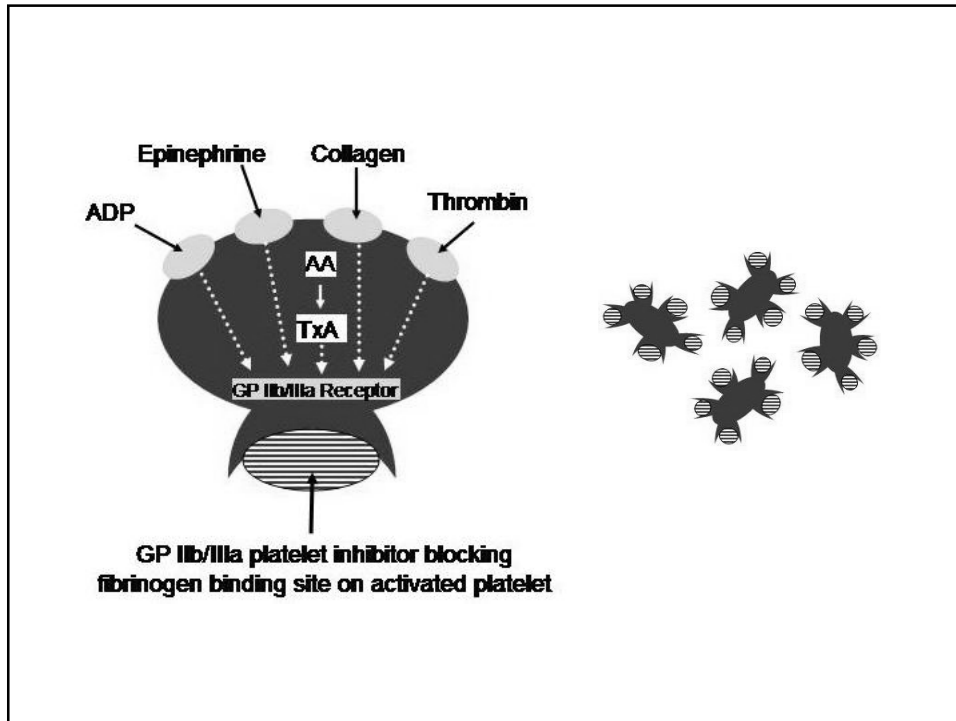
- Norepinephrine [Levophed]
- Dopamine (high dose)
- Neosynephrine
- Epinephrine
- Vasopressin

Pathogenesis of ACS



Drug Sites of Action



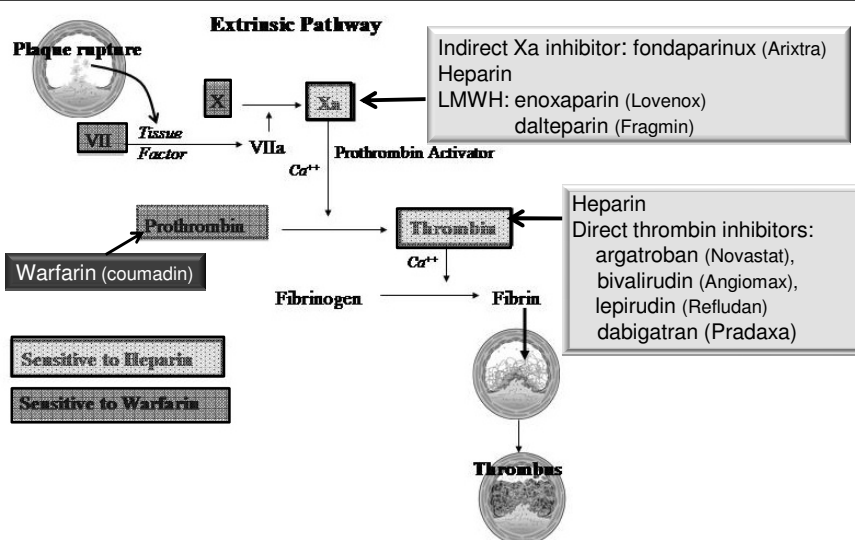


Platelet Inhibitors	
<p>Inhibit Platelet Activation</p> <ul style="list-style-type: none"> • ASA • Clopidogrel (Plavix) • Prasugrel (Effient) • Heparin • Angiomax 	<p>Inhibit Platelet Aggregation</p> <ul style="list-style-type: none"> • IIb/IIIa Inhibitors <ul style="list-style-type: none"> • Abciximab (Reopro) • Eptifibatide (Integrilin) • Tirofiban (Aggrastat)

Indications for Anticoagulation

- DVT prophylaxis and treatment
- Treatment of pulmonary embolus
- Prevention of embolic stroke
 - Atrial fibrillation/flutter
 - Prosthetic valves
- Management of ACS
 - Adjunct to PCI procedures
 - Given with fibrinolytic therapy
 - Unstable angina/NSTEMI

Anticoagulants



Anticoagulants

Heparins

Heparin (UFH)	<ul style="list-style-type: none"> • Long chain: binds to antithrombin to inhibit thrombin, factor Xa, others • Does not inhibit clot-bound thrombin • Given IV or SQ • Variable patient response and dosing • Monitored by aPTT (1.5-2.5 times control); platelet counts • Antidote = protamine • Can cause HIT
LMWH <ul style="list-style-type: none"> • Enoxaparin (Lovenox) • Dalteparin (Fragmin) 	<ul style="list-style-type: none"> • Short chain: inhibits factor Xa • More consistent anticoagulant effect, good correlation between response and body weight, longer effect • No lab monitoring needed; can monitor anti-Xa activity • Given SQ once or twice daily • Much less likely to cause HIT • Equivalent to UFH for most indications

Direct Thrombin Inhibitors:

- Argatroban (Novostat)
- Bivalirudin (Angiomax)
- Lepirudin (Refludan)
- Dabigatran (Pradaxa)

- Specific for both soluble and clot-bound thrombin
- More predictable response than heparin
- Do not cause HIT, can be used to treat HIT
- Monitored by aPTT
- Given IV (dabigatran is oral)
- Used in treatment and prophylaxis of DVT, prevention of embolic stroke in patients with atrial fibrillation, acute management of unstable angina or MI

Indirect Factor Xa Inhibitors:

- Fondaparinux (Arixtra)

Direct Factor Xa

Inhibitor: rivaroxiban
(not FDA approved)

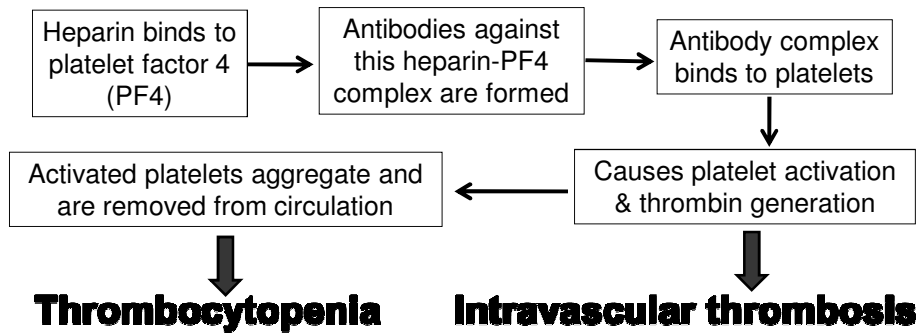
- Binds to antithrombin to inhibit factor Xa
- No platelet effect
- Does not cause HIT
- Given SQ
- No routine monitoring required; can monitor Xa activity
- No antidote known

Warfarin (Coumadin)

- Inactivates vitamin K in liver, interferes with production of prothrombin and other clotting factors
- Delayed effect (2-7 days) until existing clotting factors are cleared; heparin therapy should overlap 4-5 days
- Monitored by INR, target depends on condition being treated: 2-3 for DVT or PE, 2.5-3.5 for valves

Heparin Induced Thrombocytopenia (HIT)

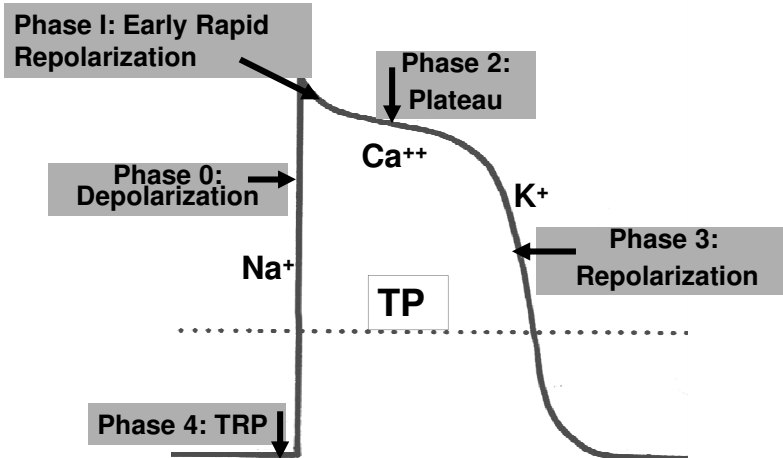
- Immune-mediated disorder that occurs 4-10 days after heparin started
- Incidence is 1-3%
- 30-80% incidence of thromboembolic sequelae



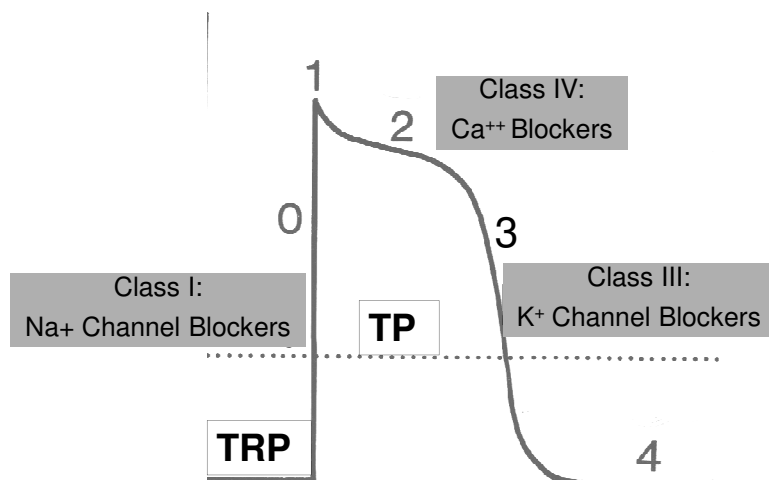
Prevention/Management of HIT

- Prevention
 - Avoid UFH when possible: LMWH, fondaparinux
 - Limit use to < 5 days
- Stop all forms of heparin
 - No heparin coated catheters
- If anticoagulation still necessary
 - Direct thrombin inhibitors: lepirudin (Refludan), argatroban (Novastat), bivalirudin (Angiomax)
 - Factor Xa inhibitor: fondaparinux (Arixtra)

Cardiac Action Potential



Antiarrhythmic Drug Sites of Action



Antiarrhythmic Drugs

Class	Examples
IA	Quinidine Procainamide (Pronestyl) Disopyramide (Norpace)
IB	Lidocaine Mexilitine
IC	Propafenone (Rhythmol) Flecainide (Tambocor)
II	Beta blockers ("olols")
III	Amiodarone Sotalol (Betapace) Ibutilide (Corvert) Dronedarone (Multaq) Dofetilide (Tikosyn)
IV	Calcium channel blockers: Verapamil, Diltiazem

Class	Action	ECG Effect
IA	Sodium channel blockade Prolong repolarization time Slow conduction velocity Suppress automaticity	↑QRS ↑QT
IB	Sodium channel blockade Accelerate repolarization	↓QT
IC	Sodium channel blockade Marked slowing of conduction No effect on repolarization	↑↑QRS
II	Beta blockade	↓HR ↑PR
III	Potassium channel blockade Prolong repolarization time	↑QT
IV	Calcium channel blockade	↓HR ↑PR

Amiodarone

- Indications
 - Ventricular arrhythmias (only FDA approved indication)
 - Conversion of atrial fib to NSR
 - Maintenance of NSR
 - Slow conduction through accessory pathway
- IV Administration
 - 1000 mg over first 24 hours given as follows:
 - First rapid infusion: 150 mg over first 10 min (15 mg/min)
 - Then: 360 mg over next 6 hours (1 mg/min)
 - Maintenance infusion: 540 mg over next 18 hours (0.5 mg/min)
 - Peripheral concentration not to exceed 2 mg/ml

Amiodarone Side Effects

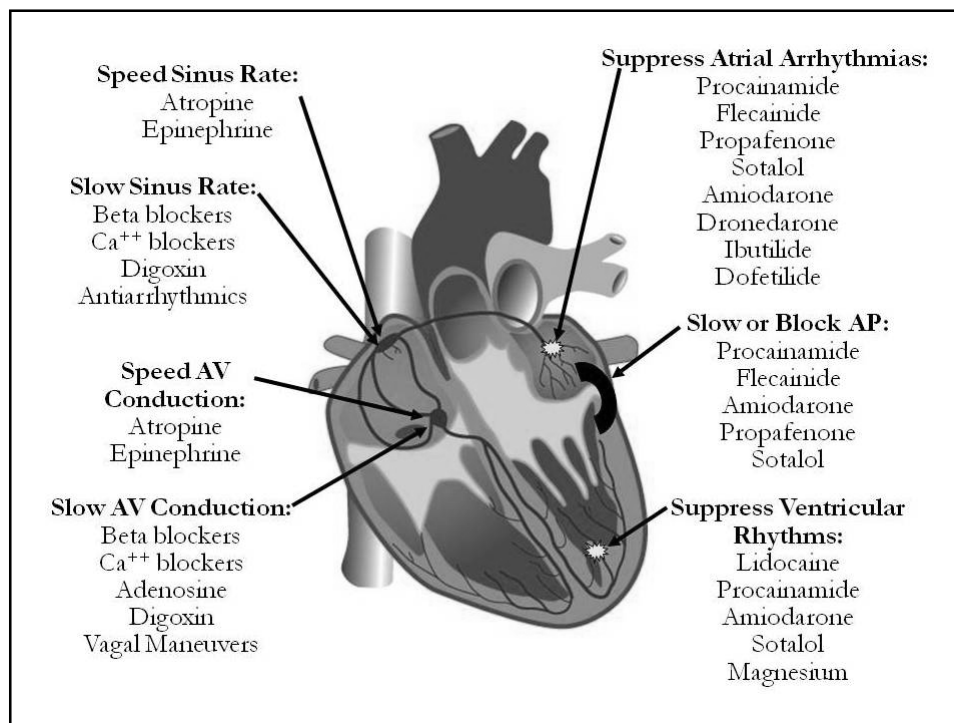
- Bradycardia
- AV block
- Proarrhythmia
- Hypotension (IV form)
- Pulmonary fibrosis
- Thyroid dysfunction (hypo & hyper)
- Liver dysfunction
- Corneal microdeposits
- Photosensitivity
- Blue skin tone
- Tremor, poor coordination
- GI upset

Unusual features

- Half life = 26 - 107 days (average = 53 days)
- Takes several weeks to achieve therapeutic levels orally
- Takes several weeks for drug levels to decrease when DCd

Baseline tests

- Chest X-ray
- Renal, liver, thyroid, pulmonary function tests



Drug Therapy for Dyslipidemias

Drug	Examples	Effects
Bile Acid Sequestrants	Cholestyramine Cholestipol, Colesevelam	Lower LDL 10-15% Slight increase HDL No change in TG
Nicotinic Acid	Niacin Niacin XR	Lower LDL 10-25% Raise HDL 15-35% Lower TG 25-30%
Statins (HMG CoA reductase inhibitors)	Atorvastatin, Fluvastatin Lovastatin, Pravastatin Rosuvastatin, Simvastatin	Lower LDL 20-60% Lower TG 10-33% Raise HDL 5-10%
Fibrates	Gemfibrozil Fenofibrate	Lower LDL 5-20% Lower TG 35-50% Raise HDL 15-33%
Intestinal Absorption Inhibitors	Ezetimibe (Zetia)	Lower LDL 18% No change in HDL May increase TG

Thank You!

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